

**AMENDMENTS TO THE CLAIMS:**

This listing of the claims will replace all prior listings and versions of claims in the application:

1-2 (cancelled)

3. (currently amended) A system for predicting nucleic acid three-dimensional structure, comprising a processor configured to:

- a) compute a plurality of secondary structures of a test nucleic acid;
- b) decompose said secondary structures into nucleic acid structure motifs;
- c) rank said structure motifs in a hierachal tree;
- d) identify candidate three-dimensional motif structures for said motifs from a database of known three-dimensional structure motifs;
- e) link said candidate three-dimensional motif structures in an order specified by said hierachal tree to generate a candidate three-dimensional composite structure;
- f) submit said candidate three-dimensional composite structure to an energy minimization algorithm to generate one or more refined candidate three-dimensional structures, wherein said energy minimization algorithm comprises
  - i. calculating energy minimization terms for said candidate three-dimensional composite structure, said energy minimization terms comprising bond stretching, bond angles, torsion stress, and non-bonded interactions;
  - ii. optimizing force constants, distance dependence, partial charges, and van der Waals radii parameters;
  - iii. accounting for gap penalties for insertions or deletions, if present in said candidate three-dimensional composite structure;
  - iv. accounting for one or more experimental constraints associated with said test nucleic acid, said experimental constraints comprising hydrogen bonding information, position of phosphorus

atoms, nuclear Overhauser effect information, residual dipolar coupling information, x-ray crystallographic electron density, cryo-electron microscopy information, and chemical probing information;

- v. employing distance constraints within a defined distance range but ignoring distance constraints outside of said defined distance range;
- vi. accounting for one or more nucleic acid folding thermodynamic measures, said nucleic acid folding thermodynamic measures comprising: folding entropy, solvation entropy changes, enthalpy changes, and free energy changes, and
- vii. accounting for known interactions, said known interactions comprising interactions with: proteins, metal ions, or other ligands by setting anchor points;

- g) rank said one or more refined candidate three-dimensional structures based on the calculated total energy and optionally one or more scoring parameters comprising: solvent accessible surface area, molecular density, non-bonded energy; and
- h) select a refined candidate three-dimensional structure based on best calculated energy to predict a three-dimensional structure of said test nucleic acid.

4. (currently amended) A method for generating a three-dimensional structure of a test nucleic acids, comprising the step of submitting a test sequence to ~~thea system of claim 3 for predicting nucleic acid three-dimensional structure, said system comprising a processor configured to:~~

- a) compute a plurality of secondary structures of a test nucleic acid;
- b) decompose said secondary structures into nucleic acid structure motifs;
- c) rank said structure motifs in a hierachal tree;
- d) identify candidate three-dimensional motif structures for said motifs from a database of known three-dimensional structure motifs;

- e) link said candidate three-dimensional motif structures in an order specified by said hierachal tree to generate a candidate three-dimensional composite structure;
- f) submit said candidate three-dimensional composite structure to an energy minimization algorithm to generate one or more refined candidate three-dimensional structures, wherein said energy minimization algorithm comprises
  - i. calculating energy minimization terms for said three-dimensional composite structure, said energy minimization terms comprising bond stretching, bond angles, torsion stress, and non-bonded interactions;
  - ii. optimizing force constants, distance dependence, partial charges, and van der Waals radii parameters;
  - iii. accounting for gap penalties for insertions or deletions, if present in said candidate three-dimensional composite structure;
  - iv. accounting for one or more experimental constraints associated with said test nucleic acid, said experimental constraints comprising hydrogen bonding information, position of phosphorus atoms, nuclear Overhauser effect information, residual dipolar coupling information, x-ray crystallographic electron density, cryo-electron microscopy information, and chemical probing information;
  - v. employing distance constraints within a defined distance range but ignoring distance constraints outside of said defined distance range;
  - vi. accounting for one or more nucleic acid folding thermodynamic measures, said nucleic acid folding thermodynamic measures comprising: folding entropy, solvation entropy changes, enthalpy changes, and free energy changes, and
  - vii. accounting for known interactions, said known interactions comprising interactions with: proteins, metal ions, or other ligands

by setting anchor points;

- g) rank said one or more refined candidate three-dimensional structures based on the calculated total energy and optionally one or more scoring parameters comprising: solvent accessible surface area, molecular density, non-bonded energy; and
- h) select a refined candidate three-dimensional structure based on best calculated energy to predict a three-dimensional structure of said test nucleic acid.

under conditions such that a three-dimensional structure of said test sequence is generated.

5. (currently amended) A system for generating populating a nucleic acid three-dimensional structure motif database, comprising a processor configured to:

- a) receive nucleic acid physical structure information for a three-dimensional structure of a nucleic acid;
- b) decompose said physical structure information into candidate nucleic acid three-dimensional structure motifs;
- c) associate data with said candidate nucleic acid three-dimensional structure motifs, said data comprising: type of motif, size of motif, coordinates of backbone, and dihedral angles for bases;
- d) compare said candidate nucleic acid three-dimensional structure motifs to existing motifs in said database to identify unique nucleic acid three-dimensional structure motifs; and
- e) add said unique nucleic acid three-dimensional structure motifs and associated data to said database.

6. (currently amended) A method for generating populating a nucleic acid structure motif database, comprising the step of submitting nucleic acid physical structure information to the a system of claim 5 comprising a processor configured to

- a) receive nucleic acid physical structure information for a three-dimensional

structure of a nucleic acid;

- b) decompose said physical structure information into candidate nucleic acid three-dimensional structure motifs;
- c) associate data with said candidate nucleic acid three-dimensional structure motifs, said data comprising: type of motif, size of motif, coordinates of backbone, and dihedral angles for bases;
- d) compare said candidate nucleic acid three-dimensional structure motifs to existing motifs in said database to identify unique nucleic acid three-dimensional structure motifs; and
- e) add said unique nucleic acid three-dimensional structure motifs and associated data to said database.

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7-10 (cancelled)